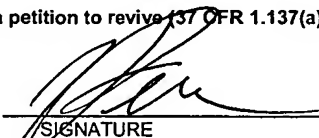


Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371</b>		ATTORNEY'S DOCKET NUMBER RTS-0428USA
		U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/511,832
INTERNATIONAL APPLICATION NO. PCT/US03/12544	INTERNATIONAL FILING DATE 04/21/2003	PRIORITY DATE CLAIMED 4/19/2002
TITLE OF INVENTION ANTISENSE MODULATION OF HYDROSTEROID 11-BETA DEHYDROGENASE 1 EXPRESSION		
APPLICANT(S) FOR DO/EO/US Susan M. Freier		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"><li>1. <input type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a submission under 35 U.S.C. 371.</li><li>2. <input checked="" type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a submission under 35 U.S.C. 371.</li><li>3. <input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</li><li>4. <input type="checkbox"/> The US has been elected (Article 31).</li><li>5. <input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))<ol style="list-style-type: none"><li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li></ol></li><li>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).<ol style="list-style-type: none"><li>a. <input type="checkbox"/> is attached hereto.</li><li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li></ol></li><li>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))<ol style="list-style-type: none"><li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li><li>d. <input type="checkbox"/> have not been made and will not be made.</li></ol></li><li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li><li>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li><li>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li></ol>		
Items 11 to 20 below concern document(s) or information included:		
<ol style="list-style-type: none"><li>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li><li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li><li>13. <input type="checkbox"/> A preliminary amendment.</li><li>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li><li>15. <input type="checkbox"/> A substitute specification.</li><li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li><li>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821- 1.825.</li><li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</li><li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li><li>20. <input type="checkbox"/> Other items or information:</li></ol>		

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) 10/511,832		INTERNATIONAL APPLICATION NO. PCT/US03/12544		ATTORNEY'S DOCKET NUMBER RTS-0428USA	
The following fees have been submitted				<b>CALCULATIONS      PTO USE ONLY</b>	
21. <input type="checkbox"/> Basic national fee..... \$300				\$	
22. <input type="checkbox"/> Examination fee If International preliminary examination report prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4)..... \$100 All other situations..... \$200				\$	
23. <input type="checkbox"/> Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority..... \$100 International Search Report prepared and provided to the Office..... \$400 All other situations..... \$500				\$	
<b>TOTAL OF 21, 22 and 23 =</b>				\$	
<input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.					
Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof (round up to a whole number)	RATE		
- 100 =	/50 =		x \$250	\$	
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(h)).				\$ 130.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$	
Total claims	- 20 =		x \$ 50	\$	
Independent claims	- 3 =		x \$200	\$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$360	\$	
<b>TOTAL OF ABOVE CALCULATIONS =</b>				\$	
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by 1/2.					
<b>SUBTOTAL =</b>				\$	
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).				\$	
<b>TOTAL NATIONAL FEE =</b>				\$	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				\$	
<b>TOTAL FEES ENCLOSED =</b>				\$ 65.00	
01/05/2006 LLANDGRA 00000038 500252 10511832 01 FC:2617 65.00 DA				Amount to be refunded:	\$
				Amount to be charged:	\$ 65.00
a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed. b. <input checked="" type="checkbox"/> Please charge my Deposit Account No. <u>56-0252</u> in the amount of \$ <u>65.00</u> to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed. d. <input type="checkbox"/> Fees are to be charged to a credit card. <b>WARNING:</b> Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.					
<b>NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed  and granted to restore the International Application to pending status.</b>					
SEND ALL CORRESPONDENCE TO: Cozen O'Connor 1900 Market Street Philadelphia, PA 19103 Telephone No.: (215) 665-6914 Facsimile No.: (215) 665-2013					
				 _____ SIGNATURE	
				_____ NAME	
				52,887 REGISTRATION NUMBER	



## UNITED STATES PATENT AND TRADEMARK OFFICE

Rec'd PG/PPC 00 JAN 2006

 UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/511,832	Susan M Freier	ISIS0048-101

INTERNATIONAL APPLICATION NO.
-------------------------------

PCT/US03/12544

I.A. FILING DATE	PRIORITY DATE
04/21/2003	04/19/2002

 Cozen O'Connor  
 1900 Market Street  
 6th floor  
 Philadelphia, PA 19103-3508

CONFIRMATION NO. 2330

371 FORMALITIES LETTER



\*OC000000017332635\*

Date Mailed: 10/28/2005

### NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 10/19/2004
- Copy of the International Search Report filed on 10/19/2004
- Preliminary Amendments filed on 10/19/2004
- Biochemical Sequence Diskette filed on 10/19/2004
- Oath or Declaration filed on 10/19/2004
- Biochemical Sequence Listing filed on 10/19/2004
- Request for Immediate Examination filed on 10/19/2004
- U.S. Basic National Fees filed on 10/19/2004
- Priority Documents filed on 10/19/2004
- Specification filed on 10/19/2004
- Claims filed on 10/19/2004
- Abstracts filed on 10/19/2004

The applicant needs to satisfy supplemental fees problems indicated below

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date. The current oath or declaration does not comply with 37 CFR 1.497(a) and (b) in that it:
  - is not executed in accordance with either 37 CFR 1.66 or 37 CFR 1.68.
- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.492(h) of \$130 for a non-small entity, must be submitted with the

missing items identified in this letter.

**SUMMARY OF FEES DUE:**

Total additional fees required for this application is \$130 for a Large Entity:

- \$130 Surcharge.

**ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.**

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

FREDERICK SMITH

Telephone: (703) 308-9140 EXT 210

**PART 1 - ATTORNEY/APPLICANT COPY**

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/511,832	PCT/US03/12544	ISIS0048-101

FORM PCT/DO/EO/905 (371 Formalities Notice)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

## Certificate of Mailing under 37 CFR 1.8

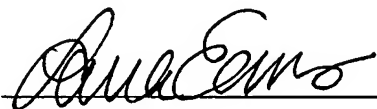
Items Included in this Mailing:

Response to Notification of Missing Requirements; Executed Declaration and Power of Attorney;  
 Copy of Notification of Missing Requirements

I hereby certify that the above correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop PCT  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, VA 22313-1450

on December 28, 2005  
 Date



Signature

Laura Eames

Typed or printed name of person signing Certificate

N/A

Registration Number, if applicable

760-603-2553

Telephone Number

Note: Each paper must have its own certificate of mailing, or this certificate must identify each submitted paper.

This collection of information is required by 37 CFR 1.8. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1.8 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.